

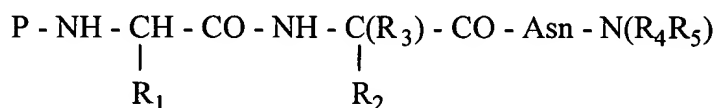
ATTACHMENT B

Amendments to the Claims

Please cancel claims 26-28 without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A pseudopeptide having general formula I



wherein:

P denotes a protecting group or a hydrogen atom,

R₁ denotes:

a phenylmethyl radical wherein the phenyl nucleus is substituted in the para position by -OPO₃H₂, phosphonomethyl, phosphonomonofluoromethyl or phosphonodifluoromethyl radical or

a ~~naphthylemethyl~~ naphthylmethyl radical which may be substituted in the 4 position by -OPO₃H₂, phosphonomethyl, phosphonomono- or phosphonodifluoromethyl radical, each of these radicals also being optionally substituted by one or more substituents selected from among the C₁ to C₄ alkyl or C₁ to C₄ alkoxy groups and/or one or more halogen atoms,

R₂ denotes:

a phenylmethyl or ~~naphthylemethyl~~ naphthylmethyl or cyclohexylmethyl radical, 2- or 3-pyridinylmethyl, substituted at the para or meta position of the ring

by -OPO₃H₂, C₁ to C₂ phosphonoalkyl group, phosphonomonofluoromethyl, phosphonodifluoromethyl, -OPO₃H₂ -PO₃H₂, phosphinate, -Se₃H -SO₃H sulfonomethyl, -CO₂H, carboxymethyl, carboxymethyloxy, malonyl, 2-(dicarboxy)ethyl, 2-malonyloxy, 5-tetrazolyl or 5-tetrazolylmethyl radical or a radical alkyl of the type (CH₂)_n (wherein n = 3 or 4) substituted in end position by a -OPO₃ H₂, C₁ to C₂ phosphonoalkyl, preferably phosphonomonofluoromethyl and phosphonodifluoromethyl, phosphonate, phosphinate, sulfonate, sulfonomethyl, carboxylate, carboxymethyl, carboxymethyloxy, malonyl, 2-malonyloxy, 2-dicarboxyethyl, 5-tetrazolyl or 5-tetrazolylmethyl radical,

R₃ denotes a straight chain or branched C₁ to C₄ alkyl group or an alkylcycloalkyl group having a C₃ to C₆ cycloalkyl,

R₄ and/or R₅ denote:

- a hydrogen,
- a straight chain or branched C₁ to C₆ alkyl group
- a C₁ to C₆ arylalkyl group wherein aryl denotes a phenyl or naphthyl nucleus optionally substituted by one or more hydroxyl groups, or
- an aminohexanoic chain followed by the sequences

RQIKIWFQNRRMKWKK (SEQ ID NO: 1), IRQPKIWFPNRRKPWKK (SEQ ID NO: 2), Cys-S-S-Cys-RQIKIWFQNRRMKWKK (SEQ ID NO: 3) and Cys-S-S-Cys-IRQPKIWFPNRRKPWKK (SEQ ID NO: 4) derived from Antennapedia or pharmaceutically acceptable salts thereof.

2. (Currently Amended) The ~~pseudopeptide~~ pseudopeptide according to claim 1, wherein:

P denotes an RCO or ROCO group where R denotes a C₁₋₄ aminoalkyl or C₁₋₄ aminophenylalkyl,

R₁ denotes a phenylmethyl group substituted in the para position by a substituent selected from among OPO₃H₂, CH₂PO₃H₂, CHFPO₃H₂ and CF₂PO₃H₂,

R₂ denotes a phenylmethyl group substituted in the meta or para position by -OPO₃ H₂, C₁ to C₂ phosphonoalkyl group, phosphonomonofluoromethyl, phosphonodifluoromethyl, phosphonate, phosphinate, -SO₃H, sulfonomethyl, -CO₂H, carboxymethyl, carboxymethyloxy, malonyl, 2-(dicarboxy)ethyl, 2-malonyloxy, 5-tetrazolyl or 5-tetrazolylmethyl radical,

R₃ denotes a C₁ to C₄ alkyl group,

R₄ and/or R₅ denote a hydrogen atom, an alkyl (CH₂)_n-CH₃ or (CH₂)_n-Ar group wherein Ar denotes a phenyl or α or β-naphthyl which may or may not be substituted and n is between 0 and 5 and pharmaceutically acceptable salts thereof.

3. (Previously Presented) The pseudopeptide according to claim 1, wherein:

R₁ denotes a phenylmethyl group having -OPO₃ H₂ group in the para-position,

R₂ denotes a phenylmethyl group having, in the para- or meta-position, a group selected from the group consisting of a phosphate, phosphonomethyl, 2-malonyloxy or (CH₂)_nCO₂H group wherein n is equal to 0 or 1,

R₃ denotes a C₁-C₄ alkyl group, and

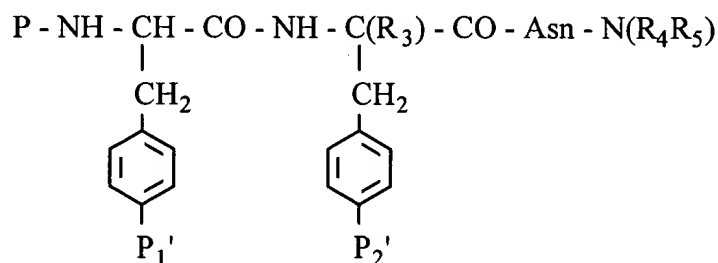
R₄ and R₅ both represent a hydrogen atom and the pharmaceutically acceptable salts thereof.

4. (Previously Presented) The pseudopeptide according to claim 1 selected from the group consisting of:

- mAZ-pTyr-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)pTyr-Asn-Aha-Antennapedia
- mAZ-Pmp-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(CH₂-COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)F₂Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe (PO₃ H₂)-Asn-Aha-Antennapedia.

5-21. (Cancelled)

22. (Previously Presented) A pseudopeptide compound corresponding to general formula II



II

wherein:

P denotes a protecting group or a hydrogen atom,

R₃ denotes a straight chain or branched C₁ to C₄ alkyl group or an alkylcycloalkyl group having a C₃ to C₆ cycloalkyl,

R₄ and/or R₅ denote

a hydrogen,

a straight chain or branched C₁ to C₆ alkyl group

a C₁ to C₆ arylalkyl group wherein aryl denotes a phenyl or naphthyl nucleus

optionally substituted by one or more hydroxyl groups, or

an aminohexanoic chain followed by the sequences RQIKIWFQNRRMKWKK

(SEQ ID NO: 1), IRQPKIWFPNRRKPWKK (SEQ ID NO: 2, Cys-S-S-Cys-

RQIKIWFQNRRMKWKK (SEQ ID NO: 3) and Cys-S-S-Cys-

IRQPKIWFPNRRKPWKK (SEQ ID NO: 4), derived from Antennapedia,

P₁' is mono or bis-(S-acyl-2-thioethyl) phosphate and/or mono or bis-

(acyloxymethyl) phosphate group wherein the term acyl denotes a tert-butylcarbonyl or isopropylcarbonyl or acetyl group; or

mono is bis-(s-acyl-2-thioethyl) phosphate and/or mono or bis-(acyloxymethyl) phosphate group wherein the term acyl denotes a tert-butylcarbonyl or isopropylcarbonyl or acetyl group; or

P₂' is mono or bis-(S-acyl-2-thioethyl) phosphate and/or mono or bis-(acyloxymethyl) phosphonomethyl groups wherein the term acyl denotes a tert-butylcarbonyl or isopropylcarbonyl or acetyl group; or

mono or bis-(S-acyl-2-thioethyl) phosphonomethyl and/or mono or bis-(acyloxymethyl) phosphonomethyl groups wherein the term acyl denotes a tert-butylcarbonyl or isopropylcarbonyl or acetyl group,

mono or bis-(S-acyl-2-thioethyl) phosphonate and/or mono or bis-(acyloxymethyl) phosphonate group wherein the term acyl denotes a tert-butylcarbonyl or isopropylcarbonyl or acetyl group, or

in the form of a carbonxylate of:

arylalkyl where the term aryl denotes a benzene nucleus and the term alkyl denotes a straight or branched carbon chain having 1 to 3 carbon atoms;

morpholinyl alkyl – (CH₂)_n (NC₄H₈O);

piperidinyl alkyl –(CH₂)_n(NC₅H₁₀) optionally substituted by and OH, CO₂H, CO₂R' where R' is a straight or branched alkyl chain which may or may not contain a benzyl or phenyl group;

piperazinylalkyl – (CH₂)_n(NC₄H₈NH) optionally substituted by (-N-C₄H₈-NR'') where R'' denotes an alkyl chain containing 1 to 6 carbon atoms, a benzyl group or a phenyl group, wherein n is between 1 and 3.

23. (Currently Amended) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 1, ~~in an amount effective to inhibit proliferation of tumor cells.~~

24. (Currently Amended) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 1, selected from the group consisting of :

- mAZ-pTyr-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)pTyr-Asn-Aha-Antennapedia
- mAZ-Pmp-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(G₂-COOH)(CH₂-COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)F₂Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)-Asn-Aha-Antennapedia.

25. (Currently Amended) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 22, ~~in an amount effective to inhibit proliferation of tumor cells.~~

26-28. (Canceled)

29. (New) A method for binding Grb2 comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1.
30. (New) A method of inhibiting activation of Ras comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1.
31. (New) A method of treating breast cancer comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1.
32. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 1, in an amount effective to bind to Grb2.
33. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 1, in an amount effective to inhibit Ras activity.
34. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 1, in an amount effective to treat breast cancer.
35. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 22, in an amount effective to bind to Grb2.
36. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 22, in an amount effective to inhibit Ras activity.

37. (New) A composition comprising a pharmaceutically acceptable carrier, and a pseudopeptide according to claim 22, in an amount effective to treat breast cancer.

38. (New) A method for binding Grb2 comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1, selected from the group consisting of:

- mAZ-pTyr-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)pTyr-Asn-Aha-Antennapedia
- mAZ-Pmp-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(CH₂-COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)F₂Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)-Asn-Aha-Antennapedia.

39. (New) A method of inhibiting Ras activity comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1, selected from the group consisting of:

- mAZ-pTyr-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)pTyr-Asn-Aha-Antennapedia
- mAZ-Pmp-(α Me)pTyr-Asn-NH₂

- mAZ-pTyr-(α Me)Phe(COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(CH₂-COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)F₂Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)-Asn-Aha-Antennapedia.

40. (New) A method of treating breast cancer comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 1, selected from the group consisting of:

- mAZ-pTyr-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)pTyr-Asn-Aha-Antennapedia
- mAZ-Pmp-(α Me)pTyr-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(CH₂-COOH)-Asn-NH₂
- mAZ-pTyr-(α Me)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)F₂Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)Pmp-Asn-NH₂
- mAZ-pTyr-(α Me)Phe(PO₃H₂)-Asn-Aha-Antennapedia.

41. (New) A method for binding Grb2 comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 22.

42. (New) A method of inhibiting activation of Ras comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 22.

43. (New) A method of treating breast cancer comprising administering to a patient in need thereof an effective amount of a pseudopeptide according to claim 22.